Pesticide Assessment Report

Glyphosate

July, 2016
Pesticides Expert Committee, Food Safety Commission of Japan

Contents

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<Background of deliberation>

- Matters concerning soft drinks -

July 1, 2003:	Request by the Minister of Health, Labour and Welfare on Assessment of the Effect of Food on Health concerning the revision of the standard for soft drinks (Shoku-An No. 0701015, Safety Division, Department of Food Safety, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare)
July 3, 2003:	Receipt of relevant documents (Reference (1)-(5) 1)
July 18, 2003:	3rd Meeting of Food Safety Commission of Japan (explanation on requested matters)
October 8, 2003:	Receipt of additional documents (Reference (1)-(5) 2) (Identification of 93 requested pesticides including glyphosate)
October 27, 2003:	1st Meeting of Pesticides Expert Committee
January 28, 2004:	6th Meeting of Pesticides Expert Committee
January 12, 2005:	22nd Meeting of Pesticides Expert Committee
April 9, 2013:	Withdrawal by the Minister of Health, Labour and Welfare on Assessment of the Effect of Food on Health concerning the revision of the standard for soft drinks (Shoku-An 0409 No. 1, Department of Food Safety, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare), and receipt of relevant documents (Reference (1) 13, (2)(3) 15, (4)(5) 11)
April 15, 2013:	471st of Food Safety Commission of Japan (explanation on withdrawal)

- Matters concerning the positive list system -

September 22, 1980:	First agricultural chemical registration
November 29, 2005:	Notification concerning Maximum Residue Limits (Reference 3)
December 19, 2008:	Request concerning the establishment of import tolerance (recombinant soybean) [2)]
February 15, 2010:	Request by the Minister of Health, Labour and Welfare on Assessment of the Effect of Food on Health concerning the establishment of the maximum residue limit (Shoku-An 0215 No. 80, Department of Food Safety, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare)
February 16, 2010:	Receipt of relevant documents (References (1) 4, 5, (2)-(4) 4-6, (5) 4)

February 18, 2010:	320th Meeting of Food Safety Commission of Japan (explanation on requested matters)
March 10, 2010:	Request concerning the establishment of import tolerance (recombinant maize) [2)]
April 7, 2010:	Request concerning the establishment of import tolerance (adzuki beans, grapes and sugar beets) [1)]
May 17, 2010:	Receipt of additional documents (Reference (1) 6-8, (2) 7, 8)
June 18, 2010:	Contact from the Ministry of Agriculture, Forestry and Fisheries to the Ministry of Health, Labour and Welfare concerning application for pesticide registration and request for the establishment of the standard (New: wheats, cabbages, etc.) [5)]
June 24, 2010:	Receipt of additional documents (Reference (5) 6, 7)
June 21, 2010:	Request by the Minister of Agriculture, Forestry and Fisheries on Assessment of the Effect of Food on Health concerning the establishment of the maximum residue limit in feed (22 Sho-an No. 2702, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries)
June 22, 2010:	Receipt of relevant documents (Reference (1)(2) 9, 10, (3)(4) 7, (5) 5)
June 24, 2010:	337th Meeting of Food Safety Commission of Japan (explanation on requested matters)
October 13, 2010:	2nd meeting, Assessment Subcommittee 4, Pesticides Expert Committee[1)]
October 22, 2010:	3rd meeting, Assessment Subcommittee 1, Pesticides Expert Committee[2)]
November 2, 2010:	3rd meeting, Assessment Subcommittee 4, Pesticides Expert Committee[3)]
November 17, 2010:	4th meeting, Assessment Subcommittee 3, Pesticides Expert Committee[4)]
December 22, 2010:	4th meeting, Assessment Subcommittee 1, Pesticides Expert Committee[5)]
April 5, 2011:	Receipt of additional documents (Reference (1) 11-13)
August 8, 2011:	Receipt of additional documents (Reference (2) 11-13)

November 9, 2011: Receipt of additional documents (Reference (4) 9, 10)

November 14, 2011: Receipt of additional documents (Reference (5) 9, 10)

December 4, 2012: Receipt of additional documents (Reference (3) 9-11)

December 20, 2012: 23rd meeting, Assessment Subcommittee 4, Pesticides Expert Committee [3)]

February 7, 2013: Request concerning the establishment of import tolerance (recombinant canola) [2)]

February 12, 2013: Receipt of relevant documents (Reference (2) 14)

February 26, 2015: Receipt of additional documents (Reference (3) 12, 13)

March 19, 2015: 43rd meeting, Assessment Subcommittee 4, Pesticides Expert Committee [3)]

January 27, 2016: Request concerning the establishment of import tolerance (cottonseed, sunflower, etc.) [1)]

January 28, 2016: Receipt of additional documents (Reference (1) 14, 15)

February 8, 2016: 133rd Review Coordinators meeting, Pesticides Expert Committee

March 24, 2016: 134th Review Coordinators meeting, Pesticides Expert Committee

April 5, 2016: Reported to the 601st Food Safety Commissioners meeting

April 6 – May 5, 2016: Public comment period

June 22, 2016: 137th Review Coordinators meeting, Pesticide Expert Committee

July 6, 2016: Reported from Chairperson of Pesticide Expert Committee to the Chairperson of Food Safety Commission

[1-5)]: Respectively concerning glyphosate (1)-(5)

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**: From 01March, 2011
***: From 23 June, 2011

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**: From 01October, 2013

From 01April, 2014

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There are multiple manufacturers of the technical material of amino acid type herbicide "glyphosate," and toxicology studies were conducted with test substances of respective sourcesrespective technical materials. For that reason, overall assessment was performed after the the combination of the technical materials and their relevant toxicology studies were individually assessed as glyphosate (1)-(5).

Individual assessment is shown in Chapter 1 to 5, and test results in livestock animals are shown in Chapter 6.

In addition, following the classification in July 2015 by IARC as "Probably carcinogenic to humans" (Group 2A), the Pesticides Expert Committee, Food Safety Commission of Japan discussed how to position the classification..

IARC conducts assessment for hazard identification using scientific reports, etc., that are publicly available to ensure fairness and transparency. On the other hand, risk assessment organizations including the Pesticides Expert Committee, Food Safety Commission of Japan, aim to assess risks in humans using mainly test results performed as GLP studies according to test guidelines that are agreed internationally, and it was confirmed that glyphosate is also assessed and concluded in the same method as other pesticides. Additionally, "Assessment by international organizations, etc." is provided for reference, including a summary of assessments by IARC and EFSA completed recently..

1. Summary of subject pesticide

(1) Nonproprietary name of active ingredient

Glyphosate (ISO common name)

Glyphosate- isopropylammonium (ISO common name)

Glyphosate- ammonium (ISO common name)

Glyphosate- potassium (ISO common name)

(2) Chemical name

Glyphosate

IUPAC

N-(phosphonomethyl)glycine

CAS (No. 1071-83-6)

N-(phosphonomethyl)glycine

Glyphosate-isopropylammonium

IUPAC

isopropylammonium *N*-(phosphonomethyl)glycinate

CAS (No. 38641-94-0)

N-(phosphonomethyl)glycine compound with 2-propanamine (1:1)

Glyphosate- ammonium

IUPAC

ammonium *N*-[(hydroxyphosphinato)methyl]glycine

CAS (No. 40465-66-5)

N-(phosphonomethyl)glycine monoammonium salt

Glyphosate-potassium

IUPAC

potassium *N*-[(hydroxyphosphinato)methyl]glycine

CAS (No.70901-12-1, 39600-42-5)

N-(phosphonomethyl)glycine monopotassium salt

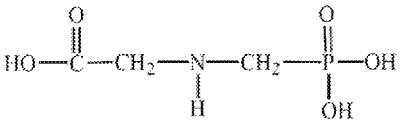
(3) Molecular formula

Glyphosate: $C_3H_8NO_5P$
Glyphosate- isopropylammonium: $C_6H_{17}N_2O_5P$
Glyphosate- ammonium: $C_3H_{11}N_2O_5P$
Glyphosate- potassium: $C_3H_7KNO_5P$

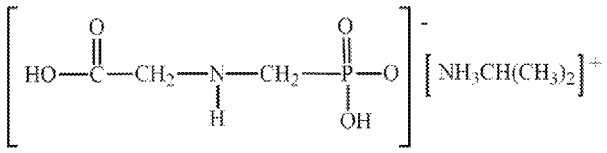
(4) Molecular weight

Glyphosate: 169.1
Glyphosate isopropylammonium: 228.2
Glyphosate ammonium: 186.1
Glyphosate potassium: 207.2

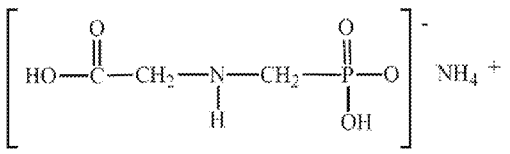
(5) Structural formula



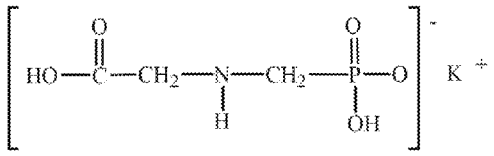
Glyphosate



Glyphosate- isopropylammonium



Glyphosate- ammonium



Glyphosate -potassium

2. Summary of assessment of glyphosate (1)

Assessment of the Effect of Food on Health regarding "Glyphosate" (CAS No. 1071-83-6) [glyphosate-ammonium (CAS No. 40465-66-5), glyphosate-isopropylammonium (CAS No. 38641-94-0) and glyphosate-potassium (CAS No. 70901-12-1)] was performed using various documents.

Study results used in assessment included animal metabolic fate (rat and rabbit), plant metabolic fate (soybean, grape, etc.), residues in crops, subacute toxicity (rat, mouse and dog), chronic toxicity (dog), combined chronic toxicity/carcinogenicity (rat), carcinogenicity (mouse), 2-generation reproduction (rat), developmental toxicity (rat and rabbit), and genotoxicity.

From the results of toxicity studies, the effects of glyphosate treatment were observed mainly in the gastrointestinal tract (diarrhea, soft stool, etc.) and body weight (reduced weight gain). No carcinogenicity, reproductive effect, teratogenicity or genotoxicity was observed.

From the results of various studies, the definition of residue: substance for dietary exposure evaluation in agricultural commodities was established as glyphosate (parent compound only).

The acceptable daily intake (ADI) of 0.75 mg/kg body weight/day was established based on developmental toxicity in rabbits at 75 mg/kg body weight/day, which was the lowest no-observed-adverse-effect-level (NOAEL) among the test results, divided by the safety

factor 100.

It was judged that there was no need to establish the acute reference dose (ARfD) because the lowest no-observed-adverse-effect-level concerning the toxic effect that may be caused by single oral treatment, etc. with glyphosate was 1,000 mg/kg body weight obtained in acute toxicity in mice, which was not less than the cutoff (500 mg/kg body weight).

3. Summary of assessment of glyphosate (2)

Assessment of the Effect of Food on Health regarding "Glyphosate" (CAS No. 1071-83-6) [glyphosate-potassium (CAS No. 39600-42-5)] was performed using various documents.

Study results used in assessment included animal metabolic fate (rat), plant metabolic fate (paddy rice, lemon, etc.), residues in crops, etc., subacute toxicity (rat and dog), subacute neurotoxicity (rat), chronic toxicity (rat and dog), combined chronic toxicity/carcinogenicity (rat and mouse), 2-generation reproduction (rat), developmental toxicity (rat and rabbit), and genotoxicity.

From the results of toxicity studies, the effects of glyphosate treatment were observed mainly in body weight (reduced weight gain) and the liver (elevated ALT and ALP , etc.). No neurotoxicity, carcinogenicity, reproductive effect, teratogenicity or genotoxicity was observed.

The definition of residue: substances for dietary exposure evaluation in agricultural commodities were established as glyphosate and *N*-acetylglyphosate based on the results of various studies.

The lowest no-observed-adverse-effect-level among the various test results was 100 mg/kg body weight/day in the developmental toxicity test in rabbits and this was used as the basis and was divided by the safety factor 100 to give 1 mg/kg body weight/day, which was established as the acceptable daily intake (ADI).

It was judged that there was no need to establish the acute reference dose (ARfD) because the lowest no-observed-adverse-effect-level concerning the toxic effect that may be caused by single oral treatment, etc. with glyphosate was 1,000 mg/kg body weight obtained in the acute neurotoxicity test in rats, which was not less than the cutoff (500 mg/kg body weight).

4. Summary of assessment of glyphosate (3)

Assessment of the Effect of Food on Health regarding "Glyphosate" (CAS No. 1071-83-6) [glyphosate-isopropylammonium (CAS No. 38641-94-0)] was performed using various documents.

Study results used in assessment included animal metabolic fate (rat), plant metabolic fate (rice, apple, etc.), residues in crops, etc., subacute toxicity (rat, mouse and dog), subacute neurotoxicity (rat), chronic toxicity (dog), combined chronic toxicity/carcinogenicity (rat), carcinogenicity (mouse), 2-generation reproduction (rat), developmental toxicity (rat and rabbit), and genotoxicity.

From the results of toxicity studies, the effects of glyphosate treatment were observed mainly in the gastrointestinal tract (diarrhea, intestinal dilation, intestinal mucosal hypertrophy, etc.), the kidney (renal tubular degeneration, etc.), the liver (elevated ALP, liver cell hypertrophy, etc.) and the blood (reduced RBC, etc.). No neurotoxicity, carcinogenicity, reproductive effect, teratogenicity, or genotoxicity that was a problem in the body was observed.

From the results of various studies, the definition of residue: substance for dietary exposure evaluation in agricultural commodities was established as glyphosate (parent compound only).

The lowest no-observed-adverse-effect-level among the toxicity test results was 100 mg/kg body weight/day in the 90-day subacute toxicity test (1) in rats, the 90-day subacute toxicity test and the 1-year chronic toxicity test in dogs, and this was used as the basis and was divided by the safety factor 100 to give 1 mg/kg body weight/day, which was established as the acceptable daily intake (ADI).

It was judged that there was no need to establish the acute reference dose (ARfD) because the lowest observed adverse effect level concerning the toxic effect that may be caused by single oral treatment, etc. with glyphosate was 5,000 mg/kg body weight obtained in the acute toxicity test in rats and mice, which was not less than the cutoff (500 mg/kg body weight).

5. Summary of assessment of glyphosate (4)

Assessment of the Effect of Food on Health regarding "Glyphosate" (CAS No. 1071-83-6) [glyphosate-isopropylammonium (CAS No. 38641-94-0)] was performed using various documents.

Study results used in assessment included animal metabolic fate (rat), plant metabolic fate (rice, apple, etc.), fate in soil and in water, residues in crops, subacute toxicity (rat, mouse and dog), chronic toxicity (dog), combined chronic toxicity/carcinogenicity (rat), carcinogenicity (mouse), 2-generation reproduction (rat), developmental toxicity (rat and rabbit), and genotoxicity.

From the results of toxicity studies, the effects of glyphosate treatment were observed mainly in body weight (reduced weight gain), the gastrointestinal tract (soft stool, increased cecum weight, etc.) and the blood (anemia). No carcinogenicity, reproductive effect, teratogenicity or genotoxicity was observed.

From the results of various studies, the definition of residue: substance for exposure evaluation in agricultural commodities was established as glyphosate (parent compound only).

The lowest no-observed-adverse-effect-level among the toxicity test results was 100 mg/kg body weight/day in the developmental toxicity test in rabbits, and this was used as the basis and was divided by the safety factor 100 to give 1 mg/kg body weight/day, which was established as the acceptable daily intake (ADI).

It was judged that there was no need to establish the acute reference dose (ARfD) because the lowest observed adverse effect level concerning the toxic effect that may be caused by single

oral treatment, etc. with glyphosate was 5,000 mg/kg body weight obtained in the acute toxicity test in rats and mice, which was not less than the cutoff (500 mg/kg body weight).

6. Summary of assessment of glyphosate (5)

Assessment of the Effect of Food on Health regarding "Glyphosate" (CAS No. 1071-83-6) [glyphosate-isopropylammonium (CAS No. 38641-94-0)] was performed using various documents.

Study results used in assessment included animal metabolic fate (rat), plant metabolic fate (rice, apple, etc.), residues in crops, subacute toxicity (rat and dog), subacute neurotoxicity (rat), chronic toxicity (dog), combined chronic toxicity/carcinogenicity (rat), carcinogenicity (mouse), 2-generation reproduction (rat), developmental toxicity (rat and rabbit), and genotoxicity.

From the results of toxicity studies, the effects of glyphosate treatment were observed mainly in the gastrointestinal tract (soft stool, diarrhea, etc.). No neurotoxicity, carcinogenicity, reproductive effect, teratogenicity or genotoxicity was observed.

From the results of various studies, the definition of residue: substance for dietary exposure evaluation in agricultural commodities was established as glyphosate (parent compound only).

The lowest no-observed-adverse-effect-level among the toxicity test results was 200 mg/kg body weight/day in the developmental toxicity test in rabbits, and this was used as the basis and was divided by the safety factor 100 to give 2 mg/kg body weight/day, which was established as the acceptable daily intake (ADI).

It was judged that there was no need to establish the acute reference dose (ARfD) because no toxic effect that may be caused by single oral treatment, etc. with glyphosate was observed.

7. Summary of studies related to residues in livestock products

(1) Animal metabolic fate test in livestock

As a result of animal metabolic fate test in livestock (lactating goats and egg-laying hens) with ^{14}C-labeled glyphosate, the major radioactive component in urine, feces, organs and tissues was unchanged glyphosate, and a small amount of B was observed among metabolites.

(2) Residues in livestock products test

As a result of the residues in livestock products test performed in Japan using glyphosate as analyte, glyphosate was detected at 0.01-0.03 μg/g in the liver of pigs in the 7.5- or 15-mg/kg treatment group, and at 0.01 μg/g in the chicken yolk of the 15-mg/kg treatment group, while it was all below the detection limit (0.01 μg/g) in the other samples (pig muscle and fat, and chicken muscle, fat and liver). It was less than 0.02 μg/g in cow milk.

As a result of the residues in livestock products test performed overseas using glyphosate and metabolite B as analytes, the maximum residues of glyphosate and B were 9.1 and 0.97 μg/g, respectively, in the porcine kidney.

(3) Definition of residue: Substance for dietary exposure evaluation in livestock products

As a result of animal metabolic fate test in livestock, metabolite B was observed, but metabolite B is also observed in rats, thus the substance for exposure evaluation in livestock products was established as glyphosate (parent compound only).

8. Assessment by international organizations, etc. (carcinogenicity)

(1) Assessment by IARC

IARC assessed the carcinogenicity of glyphosate as "Probably carcinogenic to humans" (Group 2A) because there was a limited evidence in humans based on that relationship with non-Hodgkin lymphoma was observed, and because there were sufficient evidences on carcinogenicity in laboratory animals based on test results in ICR mice and SD rats.

In addition, it was investigated upon the assessment if the carcinogenic mechanism in animal studies could also occur in humans. It was taken into account that: glyphosate products induced chromosomal damages in blood cells in a cytogenetic survey in human population; and that it was assessed that there was a strong evidence that glyphosate, glyphosate products and metabolite B induced oxidative stress in an *in vitro* test in human cells and in a test in laboratory animals. (Reference 1)

(2) Assessment by EFSA

It was concluded by EFSA that glyphosate is not carcinogenic in humans, and that there is no need for classification and labeling based on the CLP[1] regulation.

There was no statistically significant increase in the frequency of tumors in 9 studies in rats. Although an increase in malignant lymphoma was observed at the highest dose of the 1,460 mg/kg body weight/day treatment group in 1 of 5 studies performed in mice, it was not considered that glyphosate showed carcinogenicity according to the criteria based on the current guidelines. (Reference 2)

In addition, the evidence on the relationship between glyphosate products and non-Hodgkin lymphoma was very limited, and the causal relationship between glyphosate and cancer in surveys in humans was not conclusive. (Reference 2)

[1] Classification, Labelling and Packaging

Moreover, the genotoxicity results were negative in *in vitro* studies performed according to GLP and many published literature. Chromosomal aberrations, sister chromatid exchanges and DNA strand breaks were seen in some of published literature, while positive results concerning these endpoints were not observed in *in vivo* studies. On the other hand, all results were negative in *in vivo* studies in somatic cells, excluding 2 studies with intraperitoneal administration. The dose in the studies with positive results was over the LD_{50}, and thus the results were considered to be the secondary effects of cytotoxicity. As a result of overall judgment including the quality and reliability of all available studies, it was judged that glyphosate has no genotoxicity in the living body. (Reference 3)

9. Overall assessment

Glyphosate is formulated and used as ammonium salt, isopropylamine salt or potassium salt, dissociates in aqueous solution, and presents as free acid in crops after herbicide application. Based on this, the ADI and the ARfD were established on the basis of toxicity studies mainly using glyphosate (acid) in glyphosate (1)-(5), and the overall assessment of glyphosate was performed by investigating these assessments cross-sectionally. A summary of the assessment is described below:

As a result of animal metabolic fate test with ^{14}C-labeled glyphosate, the plasma radioactivity concentration after oral treatment in rats reached the C_{max} comparatively rapidly, and then rapidly attenuated. The absorption rate was considered to be at least 20%. Excretion was rapid, and the administered radioactivity was mainly excreted in feces. Unchanged glyphosate and metabolite B were observed as components in urine and feces.

As a result of animal metabolic fate test with ^{14}C-labeled glyphosate in livestock (lactating goats and egg-laying hens), the major radioactive component in urine, feces, organs and tissues was unchanged glyphosate, and a small amount of B was observed among metabolites.

As a result of plant metabolic fate test with ^{14}C-labeled glyphosate, isopropylamine salt, glyphosate-potassium, trimesium salt and sodium salt, B was observed as a metabolite over 10%TRR. In glyphosate-tolerant soybean and maize, *N*-acetylglyphosate and metabolite F were observed over 10%TRR.

Based on the results of toxicity studies with glyphosate, the effects of glyphosate treatment were observed mainly in body weight (gain suppression), the gastrointestinal tract (diarrhea, increased cecum weight, intestinal dilation, intestinal mucosal hypertrophy, etc.) and the liver (elevated ALP , liver cell hypertrophy, etc.). No neurotoxicity, carcinogenicity, reproductive effect, teratogenicity or genotoxicity was observed.

The lowest no-observed-adverse-effect-level among the toxicity test results performed with respective technical materials was 75 mg/kg body weight/day obtained in the developmental toxicity test in rabbits with glyphosate (1). Although the equivalence of the drug substances has not been shown, the Pesticides Expert Committee, Food Safety Commission of Japan judged that the no-observed-adverse-effect-level of glyphosate in the developmental toxicity test in rabbits was 100 mg/kg body weight/day considering comprehensively toxicity observations and dose settings in studies performed with the other technical materials.

Therefore, because the lowest no-observed-adverse-effect-level among the test results was 100 mg/kg body weight/day in the 90-day subacute toxicity test in rats, the 90-day subacute toxicity test and the 1-year chronic toxicity test in dogs, and the developmental toxicity test in rabbits, and this was used as the basis and was divided by the safety factor 100 to give 1 mg/kg body weight/day, which was established as the acceptable daily intake (ADI) by the Pesticides Expert Committee, Food Safety Commission of Japan.

It was judged that there was no need to establish the acute reference dose (ARfD) because the no-observed-adverse-effect-level concerning the toxic effect that may be caused by single oral treatment, etc. with glyphosate was not less than the cutoff (500 mg/kg body weight).

As a result of plant metabolic fate test and animal metabolic fate test in livestock, metabolites B and F and *N*-acetylglyphosate in plants, and metabolite B in livestock were observed as metabolites over 10%TRR. While metabolite F and *N*-acetylglyphosate were not observed in rats, the acute oral toxicity of metabolite F was mild (LD_{50}: > 5,000 mg/kg body weight) and the genotoxicity result was negative, and thus the definition of residue: substances for dietary exposure evaluation in agricultural commodities were established as glyphosate and *N*-acetylglyphosate, and the definition of residue: substance for dietary exposure evaluation in livestock products was established as glyphosate (parent compound only).

ADI	1 mg/kg body weight/day
(ADI justification document (1))	subacute toxicity test
(Animal species)	rat
(Period)	90 days
(Treatment method)	oral gavage
(ADI justification document (2))	subacute toxicity test
(Animal species)	dog
(Period)	90 days
(Treatment method)	oral capsule
(ADI justification document (3))	chronic toxicity test
(Animal species)	dog
(Period)	1 year
(Treatment method)	oral capsule
(ADI justification document (4))	developmental toxicity test
(Animal species)	rabbit
(Period)	Day 6-18 of gestation
(Treatment method)	oral gavage
(No-observed-adverse-effect-level)	100 mg/kg body weight/day
(Safety factor)	100

ARfD	Establishment not required

Exposure amount should be checked when the provisional standard is reviewed based on this assessment result.

References

<JMPR (2004)>	
ADI*	1.0 mg/kg body weight/day
(ADI justification document)	combined chronic toxicity/carcinogenicity test
(Animal species)	rat
(Period)	2 years
(Treatment method)	dietary
(No-observed-adverse-effect-level)	100 mg/kg body weight/day
(Safety factor)	100
* Group ADI of glyphosate and metabolite B	
ARfD	Establishment not required

<EFSA (2015)>	
ADI	0.5 mg/kg body weight/day
(ADI justification document)	developmental toxicity test
(Animal species)	rabbit
(Period)	Day 7-19 of gestation
(Treatment method)	oral gavage
(No-observed-adverse-effect-level)	50 mg/kg body weight/day
(Safety factor)	100
ARfD	0.5 mg/kg body weight/day
(ARfD justification document)	developmental toxicity test
(Animal species)	rabbit
(Period)	Day 7-19 of gestation
(Treatment method)	oral gavage
(No-observed-adverse-effect-level)	50 mg/kg body weight/day
(Safety factor)	100

<United States (2002)>	
cRfD	1.75 mg/kg body weight/day
(cRfD justification document)	developmental toxicity test
(Animal species)	rabbit
(Period)	Day 6-27 of gestation
(Treatment method)	oral gavage
(No-observed-adverse-effect-level)	175 mg/kg body weight/day
(Uncertainty factor)	100
aRfD	Establishment not required

(Reference 2, 4, 5)

<References>

1. IARC: Monographs on the Evaluation of Carcinogenic Risks to Humans Volume112 (2015)

2. EFSA: Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate (2015)

3. EFSA explains the carcinogenicity assessment of glyphosate (2015)

4. JMPR: "glyphosate," Pesticide residues in food - 2004 Evaluations. Part II. Toxicological. p. 95-169(2004)

5. US EPA: Federal Register/Vol. 67, No.188, 60934-60950(2002)

References used in individual assessment are listed in the section of <References> in individual assessment reports.